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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,367	08/18/2006	Carlos Garcia-Echeverria	ON/4-32910B	2344

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NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
220 MASSACHUSETTS AVENUE
CAMBRIDGE, MA 02139

EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,367	GARCIA-ECHEVERRIA ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,33-40 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,33-40 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20090325*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on July 30, 2009.

Claims 23-24, 33-40 and 43 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claims 35-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating breast tumor comprising the step of administering a compound of formula (I), does not reasonably provide enablement for a method for treatment of neoplastic diseases and immune system disorders generally; or a method for the treatment of a disease which responds to inhibition of focal adhesion kinase and/or IGF-1R; or a method for the treatment of inflammatory and/or an immune disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons from the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that 'the claims are not "reach through" claims as the claims are limited to those compounds disclosed in the present application'. This is not, however, found to

be persuasive, for the reasons already provided in the previous office action. The instant claims are drawn to "a method for treatment of neoplastic diseases and immune system disorders generally; or a method for the treatment of a disease which responds to inhibition of focal adhesion kinase and/or IGF-1R; or a method to treat an inflammatory and/or an immune disorder". The use disclosed in the specification is ZAP-70 kinase inhibitors, useful to treat a large list of diverse diseases, some of which are listed in page 20 of the specification. Test assays and procedures are provided in the specification in pages 254-260 are related to ZAP-70 kinase inhibition and it was concluded that the compounds of the invention exhibit inhibitory activity, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of the diverse disorders of the instant claims. The diseases and disorders encompassed by the instant claims include various types of tumors, CNS diseases, infectious diseases, autoimmune diseases, etc., some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same.

(The specific reasons provided in the previous office action are incorporated here by reference).

One skilled in the art of medicinal therapy recognizes that there are complex interactions between individual genetic, developmental state, sex, dietary, environmental, drug, and lifestyle factors that contribute to the carcinogenic process, making it even more challenging to have a single therapeutic agent for the treatment of diverse diseases. Rigorously planned and executed

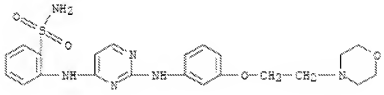
clinical trials, incorporating measurement of appropriate biomarkers and pharmacodynamic endpoints are critical for selecting the optimal dose and schedule. A detailed understanding of the molecular mode of action of the specific receptor, alongside the elucidation of the molecular pathology of individual diseases is required to identify disease types and individual patients that may benefit most from treatment. It is also important to construct a pharmacologic audit trail linking molecular biomarkers and pharmacokinetic and pharmacodynamic parameters to receptor response endpoints. Therefore, it is maintained that the specification does not enable one of skill in the art to use the claimed therapeutic method commensurate in scope, as of the filing date of the application.

2. Claims 23-24, 33-40 and 43 are rejected under 35 U.S.C. 103(a) as being obvious over Baenteli et al., WO 03/078404. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that 'examiner has not identified a reason to modify compounds of Baenteli to arrive at the presently claimed invention'. This is not, however, found to be persuasive because it was clearly provided in the previous office action that the reference teaches pyrimidine-2,4-diamine compounds that are structurally analogous to instantly claimed compounds. See the compounds of formula (I) in page 1 and the corresponding species disclosed in various tables. The compounds are taught to be useful as pharmaceutical agents, see pages 26-28. The instantly claimed compounds require a non-hydrogen substituent at the *ortho* position (or 2-position) of the ring attached to the 2-amino group of the pyrimidine (i.e., in the

claims R_{10} is required to be a non-hydrogen substituent as defined in the claims). The reference discloses pyrimidine compounds which contain substituents at the 3-, 4- and/or 5-positions, see the compounds of the examples. The instant claims differ from the reference compounds by having a substituent at a position different from the reference compounds, i.e., at the 2-position and therefore, the instantly claimed compounds are positional isomers of the reference compounds.

See, for example, the compound of Example 26 (Table 1, page 10) which has the following structure:



The instantly amended claims on the other hand require a substituent R^{10}, which is at the 2-position of the phenyl ring (with respect to the amino attachment) being a non-hydrogen substituent, including a –O-ethylene-morpholino. Accordingly, a compound according to instantly amended claims, is a structural isomer of the reference disclosed compound because it differs only by the position of the substituent on the phenyl ring.

Applicant cites *Takeda v. Alphapharm* to support the argument. However, the situation is *Takeda* is different from the instant case. The court in that case ruled that 'one of ordinary skill in the art would not have been prompted to modify the reference compound, using the steps of homologation **and** ring-walking, to synthesize the claimed compounds'. Contrary to the cited *Takeda* ruling, in the instant application, one of ordinary skill in the art needs to modify the reference compound by changing the position of a single substituent on the phenyl ring.

3. Claims 23-24, 33-40 and 43 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4 and 7-9 of copending Application No. 10/507,060.

4. Claims 23-24, 33-40 and 43 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 13-22 of copending Application No. 10/549,250.

For each of the above provisional obviousness-type double patenting rejections, the reasons provided in the previous office action are incorporated here by reference.

Applicant submits that 'the rejections will be addressed upon indication of allowable subject matter'. The rejections are maintained for the reasons provided previously.

Receipt is acknowledged of the Information Disclosure Statement filed on March 25, 2009 and a copy is enclosed herewith.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

October 27, 2009